

hormones. The W.H.O. is undertaking a programme of examination of biological agents (parasites, predators, pathogens) for controlling harmful insects and is also concerned with a large project in India to assess the possibilities of genetic control of *Culex fatigans*, the mosquito vector of filariasis.

A balanced view of these new measures suggests that none is likely to provide a universal alternative for chemical control, though many will be used separately or in combination with pesticides ("integrated control") to economize their use. Each

non-chemical method requires much expensive research and development, as do new pesticides. But if the conclusion is successful it solves only one pest problem, whereas a new pesticide may be used against many. It is to be hoped that this will not prevent the need for developing alternatives during the next decade, when we shall have to rely on chemical pesticides almost entirely.

¹ World Health Organization. *Technical Report Series*, 1970, No. 443.

² Busvine, J. R., and Pal, R., *Bulletin of the World Health Organization*, 1969, 40, 731.

Nobel Prize

This year the Nobel prize for "physiology or medicine" is awarded jointly between Sir Bernard Katz, F.R.S., professor of biophysics at University College London¹; Dr. U. von Euler, professor of physiology at the Karolinska Institute, Stockholm; and Dr. J. Axelrod, professor of pharmacology at the National Institute for Mental Health, Bethesda, U.S.A. Sir Bernard's share is for his research on the electrophysiology of neuromuscular and synaptic transmission. His first work in this field was done jointly with J. C. (now Sir John) Eccles and S. W. Kuffler in Australia about the beginning of the second world war. With external recording electrodes applied to the soleus muscle of the cat they established many of the important general features of the "endplate potential." This is the local electric response in the endplate region of muscle fibres which still occurs when neuromuscular transmission has been weakened to a point where no propagating action potential is set up in the muscle. However, he has made his main contribution by applying the intracellular microelectrode technique to these problems. This work began about 1949 and has continued ever since to produce a succession of important discoveries. He has been helped by a series of collaborators, notably P. Fatt, J. del Castillo, and R. Miledi. His experimental materials have mostly been the frog nerve-muscle preparation and the giant fibre synapse in the stellate ganglion of the squid, but most of his results have been repeated on mammalian preparations, and there is no doubt of their applicability to man.

When Katz began this series of investigations it was known that acetylcholine, released from the motor nerve terminal on the arrival of an action potential, causes a local drop in the resting potential of the muscle fibre, and if this drop is large enough it in turn sets up a propagated action potential. Katz's first work with microelectrodes (in collaboration with Fatt) analysed this process quantitatively in individual muscle fibres. They showed that acetylcholine acts by causing the muscle membrane at the endplate to become more permeable to ions, and that the endplate potential is generated by the entry of (chiefly) sodium ions which follows. It is not generated, for example, directly by the positive charge on the acetylcholine ions themselves. The change in permeability was found to be less specific for sodium ions than the change which generates the propagated action potential. This feature was used later (by Katz and del Castillo) to distinguish between the local and the propagated changes. They showed that the local change at the endplate cannot be triggered off by reduction of membrane potential, whereas in contrast the propagated change is triggered by membrane potential change but not by acetylcholine.

The next advance was the striking discovery (with Fatt) of the existence of "miniature endplate potentials." These

are changes in membrane potential similar in time course to an endplate potential but of very small and rather uniform size. In each muscle fibre they occur at irregular intervals (several per second) even when no impulses are passing down the nerve fibre. They were recognized as being due to release of acetylcholine from the nerve ending, since their amplitude and time course were affected by drugs such as curare and anticholinesterases in the same way as were the effects of applied acetylcholine. But they were much too large to be due to single molecules of acetylcholine. Even more striking than the existence of this spontaneous activity, however, was the demonstration (with del Castillo) that the endplate potential due to arrival of a nerve impulse consists of a large number (some hundreds) of these "miniature endplate potentials" occurring simultaneously. This discovery shows that neuromuscular block may be caused in several different ways: reduction of the number of "quanta" of acetylcholine released (block due to high Mg, low Ca); reduction in the amount of acetylcholine per quantum (some inhibitors of acetylcholine synthesis); or reduction of the sensitivity of the endplate to acetylcholine (curare).

Much of Katz's work in the last few years (mostly with Miledi) has been concerned with the role of calcium ions in the transmission process. It has long been known that transmission of the impulse is reduced in low-calcium solutions. Katz and Miledi have shown conclusively that the immediate cause of the release of acetylcholine quanta when the nerve impulse arrives is the entry of a small amount of calcium through the membrane of the presynaptic terminal. At present they are investigating the effects of single acetylcholine molecules, which show up as irregular fluctuations of membrane potential ("noise") at the endplate region of a muscle fibre when a small quantity of acetylcholine is applied to it.

As a result of these investigations neuromuscular transmission is probably better understood than any other cellular process of equivalent complexity. Even more important, most of the results have been shown—in many cases by Katz himself—to be relevant to synaptic as well as to neuromuscular transmission. Though very little of Katz's work has been carried out in direct relation to disease processes, it provides the immediate physiological background for everyone working on disturbances of neuromuscular and central or peripheral synaptic transmission. He has published three books,²⁻⁴ the second³ of which in particular, while a highly successful account of the fields in which he has worked, is written in a way which is intelligible to a beginner and yet carries the reader on to the boundaries of knowledge.

¹ See p. 251 for biographical note.

² Katz, B., *Electric Excitation of Nerve*. London, Oxford University Press, 1939.

³ Katz, B., *Nerve, Muscle and Synapse*. New York, McGraw-Hill, 1966.

⁴ Katz, B., *The Release of Neural Transmitter Substances*. Liverpool, Liverpool University Press, 1969.